REMARKS

I. Status Summary

Claims 1-12 are pending in the present application and are currently examined. Claims 7, 8 and 12 are withdrawn due to restriction requirement. Claims 1, 2 and 6 are herein amended. Claims 3-5 and 9-11 are canceled.

The Patent Office has stated that certain references listed in previously filed Information Disclosure Statements have not been considered. In addition, the Patent Office has made various objections to the claims and specification. Further, claims 1, 2, 4-6, and 9-11 are rejected under 35 USC § 112, second paragraph, as allegedly being indefinite. Claims 1, 2, 4-6, and 9-11 are rejected under 35 USC § 112, first paragraph, as allegedly failing to enable a person of skill in the art to use the invention and allegedly failing to adequately describe that the inventors had possession of the invention at the time of filing. Claims 1, 4, 6 and 9-11 are rejected under 35 USC § 102(b) as allegedly being anticipated by International Patent Application to Tang et al. (WO2001/57190, filed February 5, 2001; hereinafter "*Tang et al.*"). Claims 1, 2, 4, 5, 9 and 10 are rejected under 35 USC § 102(e) as allegedly being anticipated by U.S. Patent No. 6,943,241 to Isogai et al. (filed March 25, 2002 and claiming priority to November 5, 2001; hereinafter "*Isogai et al.*").

II. Information Disclosure Statement

An Information Disclosure Statement (IDS), Form 1449 and copy of the Yamada et al. reference (*Biochem. Biophys. Res. Commun.* (1999) **261**, 614-621; hereinafter "*Yamada et al.*") are submitted with this response. The *Yamada et al.* reference was one of the references listed on a Search Report included as part of the IDS submitted on May 10, 2005. The Patent Office is contending that the listing of references in the Search Report is not considered to be an IDS complying with 37 C.F.R. § 1.98. While the Patent Office has stated that the remaining two references listed on the Search Report submitted with the May 10, 2005 IDS have been considered, a copy of the *Yamada et al.* reference was not submitted and it has,

therefore, not been considered. Applicants respectfully request a withdrawal of this objection, as an IDS, Form 1449, and a copy of the Yamada et al. reference are submitted with this response.

III. Claim Amendments

Claim 1 has been amended by deletion of parts (2)-(4). Claim 1 has been further amended by insertion of the phrase "of a gene expressed specifically in hepatoma cells". Support for these amendments can be found throughout the claims and specification as filed and, in particular, at original claims 4 and 10. Claim 2 has been amended by insertion of the phrase "repress transcription of a gene expressed specifically in hepatoma cells, comprising" and the phrase "as an effective component". Support for these amendments can be found throughout the claims and specification as filed and, in particular, at original claims 1, 4 and 10. Claim 6 has been amended by insertion of the phrase "drug agent" and amended for consistency with the amendments to claims 1 and 2. Support for these amendments can be found throughout the claims and specification as filed and, in particular, at original claims 1 and 2. Accordingly, no impermissible new matter has been added by these claim amendments.

IV. Response to Objections to the Specification

The specification has been objected to because the Abstract consists of two paragraphs. The Abstract has been amended herein to consist of only one paragraph.

The Patent Office has stated that should claim 9 be found allowable, claim 10 will be objected to under 37 C.F.R. 1.75 as being a substantial duplicate thereof. Claims 9 and 10 are canceled.

Accordingly, Applicants respectfully request withdrawal of the objections to the Specification.

V. Response to Objections to the Claims

Claims 1, 2, 4-6 and 9-11 have been objected to for the phrase "a protein or a peptide" being allegedly redundant. In light of the specification, the skilled artisan would understand the meaning of "a protein or a peptide." However, to expedite prosecution, claim 1 has been amended by deletion of the phrase "or a peptide". Claims 4-5 and 9-11 are canceled.

Accordingly, Applicants respectfully request withdrawal of the objections to the claims.

VI. Response to the Rejections under 35 U.S.C. § 112, Second Paragraph.

Claims 1, 2, 4-6 and 9-11 have been rejected under 35 USC § 112, second paragraph, for allegedly failing to particularly point out and distinctly claim the subject matter. Specifically, the Patent Office is alleging that there is insufficient antecedent basis for the phrase "the functional domain" and that the phrase is unclear. In response, claim 1 has been amended by deletion of the phrase "the functional domain". Claim 6 is dependent on amended claim 1. Claim 2 is has been amended to remove the dependency on claim 1. Claims 4-5 and 9-11 are canceled. Therefore, Applicants respectfully submit that the rejection is obviated by the amendments, and respectfully request withdrawal of the § 112, second paragraph, rejection of claims 1, 2, 4-6 and 9-11.

VII. Response to the Rejections under 35 U.S.C. § 112, First Paragraph.

Claims 1, 2, 4-6 and 9-11 have been rejected under 35 USC § 112, first paragraph, for allegedly failing to comply with the enablement and written description requirements. Although applicants believe the claims are fully enabled and have adequate written description, in order to expedite prosecution of the application, pending claims 1, 2 and 6 are amended herein. With respect to amended claims 1, 2 and 6, applicants respectfully assert that for the reasons described in detail below, one of ordinary skill in the art at the time of filing of the application would have recognized the drug agents that are being claimed and would have known how to

make and use the drug agents to repress transcription of a gene expressed specifically in hepatoma cells. Therefore, the drug agents comprising a protein as an effective component having an amino acid sequence of SEQ ID NO: 1 or amino acids 303-502 of SEQ ID NO: 1 are adequately described and enabled by the instant specification.

To satisfy the written description requirement, the applicant must convey to the skilled artisan that, as of the filing date sought, the applicant was in possession of the invention. *See Falkner* v. *Inglis,* 448 F.3d 1357, 79 U.S.P.Q.2d 1001, 1007 (Fed. Cir. 2006) (citing *Vas-Cath, Inc.* v. *Mahurkar,* 935 F.2d 1555, 1563-64, 19 U.S.P.Q.2d 1111 (Fed. Cir. 1991). Applicants convey to the skilled artisan that they were in possession of a drug agent comprising a protein as an effective component that is a transcriptional repressor of a gene expressed specifically in hepatoma cells. For example, Applicants describe a protein that is a transcriptional repressor as an effective component comprising an amino acid sequence of SEQ ID NO: 1 or comprising amino acids 303-502 of SEQ ID NO: 1. Accordingly, the instant specification allows a person of ordinary skill in the art to recognize the drug agents that are being claimed, and recognition of what is being claimed suffices for compliance with the written description requirement. Therefore, applicants respectfully assert that amended claims 1, 2 and 6 are adequately supported by the instant application, and respectfully request that the rejection under 35 USC § 112, first paragraph, be withdrawn.

Further, applicants respectfully disagree with the Patent Office's allegation that one skilled in the art at the time the priority application was filed would not have known how to use the claimed drug agents. Specifically, the Patent Office contends at page 9 of the Official Action that: "No working examples are provided that demonstrate the ability of any ZHX3 protein to treat hepatoma or to alter the expression of pyruvate kinase M gene or type II hexokinase gene in any model. In response, applicants provide herewith a 37 C.F.R. § 1.132 Declaration that includes experimental data describing ZHX3 transcriptional repression of pyruvate kinase M (PKM) and type II hexokinase (HKII) genes as disclosed in the instant application.

As disclosed in the instant application, transcription of HKII and PKM genes is silent in normal hepatocytes and induced in hepatoma cells. Also disclosed in the instant application is that nuclear factor-Y (NF-Y) is a common transcription factor for both HKII and PKM, but NF-Y is not differentially expressed between normal hepatocytes and hepatoma cells. Therefore, it is disclosed in the instant application that an interacting partner of NF-Y can be responsible for the observed hepatoma cell specific gene expression of HKII and PKM. Indeed, Example 4 and Figure 9 of the instant application disclose that ZHX3 interacts with NF-YA. The functional domain comprising amino acid residues 303-502 of SEQ ID NO: 1 is described, for example, at page 3 of the instant application and at the original claims. ZHX3 transcriptional repressor activity of HKII and PKM genes in particular is described in the claims as originally filed. Accordingly, the ZHX3 transcriptional repressor activity of HKII and PKM genes is taught in the instant application in particular, for example, at pages 1-3 of the specification, at Figures 9, 10, 11 and 12, at Example 4 and at the original claims.

Therefore, applicants respectfully submit that the claimed drug agents comprising a protein that is a transcriptional repressor of a gene expressed specifically in hepatoma cells as an effective component comprising an amino acid sequence of SEQ ID NO: 1 or comprising amino acids 303-502 of SEQ ID NO: 1 are adequately enabled by the instant application. A person of ordinary skill in the art upon reading Applicants' disclosure would have known how to make and/or use the claimed drug agents. Therefore, amended claims 1, 2 and 6 comply with the enablement requirement of 35 U.S.C. § 112, first paragraph, and the rejection should be withdrawn.

VIII. Response to Rejections Under 35 U.S.C. § 102

Claims 1, 4, 6 and 9-11 are rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by *Tang et al.* Claims 1, 2, 4, 5, 9 and 10 are rejected under 35 USC § 102(e) as allegedly being anticipated by *Isogai et al.* Applicants respectfully disagree with these rejections as applied to amended and pending claims 1, 4 and 6.

Specifically, applicants respectfully assert that *Tang et al.* and *Isogai et al.* fail to disclose each and every element of applicant's claims 1, 4 and 6 and, therefore, do not anticipate claims 1, 4 and 6. Applicants' arguments with respect to the traversal of these rejections are described in detail below.

Applicants preliminarily note it is well settled that for a cited reference to qualify as prior art under 35 U.S.C. §102, each element of the claimed subject matter must be disclosed within the reference. "A claim is anticipated only if each and every element in the claim is found, either expressly or inherently described, in a single prior art reference." *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987).

The Patent Office asserts that *Tang et al.* discloses an amino acid sequence having 99% sequence identity to SEQ ID NO: 1. The Patent Office asserts that *Isogai et al.* discloses an amino acid sequence having 100% sequence identity to SEQ ID NO: 1. Neither *Tang et al.* or *Isogai et al.* disclose the transcriptional repressor activity of the protein encoded by SEQ ID NO: 1, as taught and claimed in the instant application. For example, in contrast to applicant's claims 1, 4 and 6, *Tang et al.* and *Isogai et al.* do not describe any specific function for the amino acid sequences that the Patent Office has asserted to be 99% and 100% identical SEQ ID NO: 1, respectively. *Tang et al.* and *Isogai et al.* have failed to describe applicant's disclosed usefulness of ZHX3 for repressing the expression of PKM and HKII genes, interacting with NF-YA, and as a drug agent for treating hepatoma. Therefore, the disclosures of *Tang et al.* and *Isogai et al.* fail to teach all of the elements of claims 1, 4 and 6, namely, the use of ZHX3 as an effective component of a drug agent to repress transcription of a gene expressed specifically in hepatoma cells. Accordingly, *Tang et al.* and *Isogai et al.* do not anticipate claims 1, 4 and 6, and applicants respectfully request that the rejections under 35 U.S.C. § 102(b) and 35 U.S.C. § 102(e) be withdrawn.

IX. CONCLUSION

In light of the above amendments and remarks, it is respectfully submitted that the present application is now in proper condition for allowance, and an early notice to such effect is earnestly solicited.

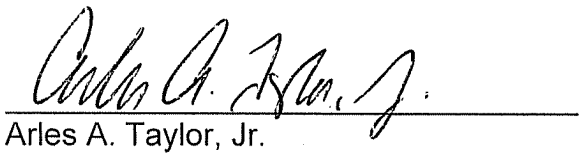
If any small matter should remain outstanding after the Patent Examiner has had an opportunity to review the above Remarks, the Patent Examiner is respectfully requested to telephone the undersigned patent attorney in order to resolve these matters and avoid the issuance of another Official Action.

DEPOSIT ACCOUNT

The Commissioner is hereby authorized to charge any fees associated with the filing of this correspondence to Deposit Account No. **50-0426**.

Respectfully submitted,

JENKINS, WILSON, TAYLOR & HUNT, P.A.

Date: 03/17/2008 By: 

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